With Compliments

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THE PRINCIPLE OF DISINFECTION IN MEDICINE,

BEING THE

INAUGURAL ADDRESS

DELIVERED ON OCTOBER 11, 1888,
ON THE OPENING OF THE FIFTIETH SESSION OF THE LIVERPOOL MEDICAL INSTITUTION.

BY THE PRESIDENT,

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THE PRINCIPLE OF DISINFECTION IN MEDICINE.

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Not the least unfortunate result of that spirit of specialism which is taking possession of the medical profession will be its tendency to obscure the view of great general principles which should at any rate be sought for as the basis of all useful practice. The acquisition of expertness in manipulative dexterity in the treatment of affections requiring the employment of special instruments absorbs so much time that the details dealt with are exalted to an undue degree of importance, and the practitioner falls into the danger of losing sight of his science in proportion to the perfection with which he learns to practise some small portion of his art. Yet, while the multiplication of instruments applicable to the investigation of particular organs, and the difficulty of acquiring expertness in their use, are tending to narrow the views of medical men to limited portions of the human body, and in that way to foster a restricted and departmental habit of mind, some of the greatest lessons that are being taught us by those who study biological phenomena in the spirit of such masters as Charles Darwin—

lessons that should be thoroughly studied by all of us—are that a thread of unity runs throughout all life upon earth associating its different forms with each other; and that in any particular form there is, in the case of every individual representing it, such a mutual subordination and interaction of all its several parts as to make it absolutely necessary that a general conception of the whole shall be constantly kept in view, if either the causes or effects of the derangement of those parts can be comprehended. Indeed, with reference to ourselves, no lesson is being more forcibly driven home to us than that the human body, in its mechanical and chemical relationships, is a variable and most complex piece of mechanism, fearfully and wonderfully built up upon a definite plan dimly foreshadowed in creatures lower than man himself; that this mechanism is capable of responding instantly, and, owing to the mutual interdependence of its several parts and the perfection of its organic self-adjustments, of responding for the most part easily, to all changes of condition; and, finally, that every readjustment finds its expression in some co-related chemical change, as is largely shown by the altered constitution of the several excreta, which can therefore be taken as a sensitive index of what is going on in the economy, and are hence deserving of the most careful study.

The second lesson mentioned above—viz., that of the mutual relation of the different parts of an organism—has been made especially comprehensible by the study of embryology. The primary apparent homogeneity of the ovular cells; the gradual differentiation of the blastoderm into epiblast, mesoblast, and hypoblast; the main but by no means entire development from each of these of systems of organs, such as the nervous system and its more intimate auxiliary mechanisms from the first, the organs of locomotion, the genito-urinary organs and vascular system from the second, as well as that connective tissue which mechanically binds all together; while from the third arises the digestive system with its ministering glands; the part which each plays in the construction of any individual organ, one contributing the glandular cells which constitutes its actively functioning portion, another the blood-vessels which are the medium of conveying to these their nourishment, and a third the tissue which cements all together—this points to an intimate fundamental relationship between structures sometimes topographically remote and on the surface dissimilar from each other, and helps us to understand what at first sight is often very puzzling, viz., how it is that tissues which in their final development are morphologically very different from each other yet react similarly to some common morbid cause—such, for example, as syphilis or gout—while other tissues immediately neighbouring some of those attacked, and resembling them closely in mere form, escape. This fundamental unity underlying external diversity, this blending of distinct embryological elements derived from each of the three great primal subdivisions of the blastoderm in the construction of even the simplest organ, points also to the necessity of studying the body as a whole even when studying any of its parts.

That even the strangest and most special aberrations from healthy structure and function are governed by general biological laws is pretty certain, and the more steadily we keep this in view, and the more we try to recognise the general in the special, the better will it be for medicine as a science. And here, as I have strayed so far from the main subject of my discourse, I may perhaps be permitted to stray a little further, and to express my belief that modern medical education does not tend to encourage the wholesome mental habit of reasoning in all cases from the special to the general; for each department, and especially each preliminary department, of study is so overcrowded with minute and technical details, the importance of which in relation to the end to be obtained—viz., the production of a clear-minded, common sense, safe, and all round helpful medical practitioner—is so magnified by its professor that the student is in danger of being lost in them as in a maze, and is often driven, as soon as he can safely disencumber himself of the main part of what he has laboriously learned, to take up with a little bit of the body, in despair of ever being able to comprehend the whole.

This is the more unfortunate because there are unmistakable indications in facts of far-reaching importance that are being presented to us by men who, for the most part, are not immediately engaged in the practice of medicine, that those of us who are thus engaged, or who propose to be so, must make a new departure, or rather, that, while availing ourselves of all that is good and really helpful in the more modern methods of investigating disease processes, we must return in principle to some of the simpler and more comprehensive views of disease itself that were entertained by the enlightened among our predecessors, and that found their expression in a nomenclature which, owing to our altered methods, is largely incomprehensible to us now. All those methods have been directed to the discovery of structural changes. Now we must return upon our path and place equally great stress upon function; and if this altered function is to be understood, it must be by a closer study than has hitherto been undertaken of those chemical changes to which I just now alluded as incessantly going on in the body, to the detection of the resulting products, the conditions of their formation, their physiological action, and the circumstances which promote or antagonise them.

It is to one aspect of this chemical side of pathology that I wish to ask your attention this evening. The title which will perhaps, on the whole, best indicate what I desire to convey will be "The Principle of Disinfection in Medicine," using the word disinfection, as will be explained, in the broadest possible sense.

There is every encouragement to investigate the chemical causes of disease. The field of structural change has been well-nigh fully explored. The advantages from the exploration, which I cannot now enlarge upon, have been very great, but they have not been unbalanced. The microscope, the stethoscope, or some one or other of our instruments of physical research demonstrates to us a structural alteration actually wrought, for this is the only kind of alteration that they can show; and that very demonstration is often of such a character as to convince us of our helplessness to do more than palliate. The morbid change has been effected. We cannot go back upon it, and despair takes the place of hope. Thus far the result is good, for it is better to know the truth than to be blundering on in darkness, and possibly hastening the inevitable issue of a fatal disease, from not having been possessed of the means of recognising its presence. But from only demonstrating structural changes, and yet from their being universally applied to the investigation of all diseases, the use of these instruments has fostered a habit of mind that tends to regard all disease as in its essence structural. Probably the truth lies much nearer the other extreme; and if we could disabuse ourselves of the belief, largely begotten of purely physical methods, that in some way or other all altered function must be the outcome of altered structure, even though in any particular case we may not be able to prove it; and if we trained ourselves to catch the import of the earlier chemical change, we should often go about our work with more of a spirit of hopefulness in ourselves, and with more likelihood of helpfulness to our patients.

For, unlike our knowledge of changes of structure, which, as I have remarked, is perhaps nearing its attainable limit, that of the chemical changes of the body is but small, and is capable of indefinite and most fruitful increase. In proof of this, if proof be needed, let me read a single passage from one of the greatest living masters in physiology:—"Of the meaning of the appearance in the tissues of such bodies as xanthin, &c., and of the exact nature of the metabolism which they undergo, we know nothing. We cannot say whether they are simply the accidental bye-products of nitrogenous metabolism—the result of imperfect chemical machinery; or whether, though small in quantity, they serve some special ends in the economy."[1] Thus writes Dr Michael Foster, or at least thus he did write in 1884. The force of the passage lies in the *et cetera;* for xanthin stands for a large number of substances, a very much larger number than that of whose sources and uses we have some fairly accurate conception. And if this is true of physiological chemistry, it is doubly so of that of disease.

[1] *Physiology*, 4th ed., p. 442.

The study of animal chemistry must therefore be extended. And the rapidly-increasing knowledge of the part played by microbes in the genesis of disease, instead of rendering this study less necessary, as from presumed notions of their action was thought likely to be the case, should really but stimulate it: for not only, or chiefly, physically, by their mere presence as bodies foreign to the human organism, nor negatively by their consumption of material designed for its nutrition, but chemically and very actively by the soluble toxic products which they actually form do they derange health. The study of these products, then,—their chemical nature, the effects which they produce, the circumstances under which they are formed, and their antidotes,—is of the utmost importance. And, using the word disinfection, as I desire to do here, as inclusive not only of antisepticism, *i.e.*, as of the results of agents which will delay the development of, even if they cannot destroy, the pathogenic microbes, but in a wider sense still, as of any agent which will prevent the noxious effects of their work, even if it does not, like an antiseptic, paralyse themselves; then we shall have to enlarge our conceptions of diet in disease, so as to consider in this sense its disinfecting power. As an indication of the kind of work that can be done in this direction, it is only necessary to allude to some suggestive experiments by Brieger, "who found that the typhoid bacillus, although it grew well in peptone, appeared to form no alkaloids from it. . . . When he cultivated it in beef-tea, however, he obtained as a product of decomposition an exceedingly small quantity of ptomaine,"[1] which, among other effects, caused, when injected into guinea-pigs, profuse diarrhœa. The bacilli were not killed by the peptone, they were not even prevented from growing and increasing; but they were rendered powerless for evil. Should not a single fact of this kind afford a powerful stimulus to renewed study of the relations of diet to some kinds of disease?

Reverting now to the opening sentence of this address, it is probably owing to the modern sharp division between medicine and surgery that the principle of disinfection, so long and so

[1] Brunton on *Disorders of Digestion*, p. 291.

successfully applied to the latter, has had but a very limited application to the former. Perhaps we may go still further, and say that the very success which attended its employment in surgery, or rather the ideas engendered by the supposed cause of that success, prevented a general extension of the principle to the treatment of internal disease. That supposed cause was the rigid employment of very special methods, which clearly could not be employed to internal parts, and hence for a long time the possible utility of other means was not considered.

An entirely new order of ideas, however, is now happily arising concerning the nature of the cause which gives immunity from any second attack of infectious disease, and hence concerning the nature of infection itself, owing to the startling results of experiments made almost simultaneously by competent physicians, residing in parts very remote from each other, and acting on animals inoculated with the infective material of several distinct diseases. How new and how strange this is, may be judged by the following quotation from Dr Lauder Brunton's book on the *Disorders of Digestion*, which was not published till 1886. "One author," he says, not even mentioning his name,[1] "has gone so far as to consider that the immunity which one attack of an infective disease confers against a subsequent one is due to alteration in the body, not by bacteria or other low organisms, but by a chemical substance which they produce, and he has proposed to afford protection against the disease by cultivating the bacteria artificially, and inoculating with the poison which they produced without the bacteria themselves. This does not seem a very promising method of treatment." That is all the comment that it was thought necessary to make, not longer ago than the year before last, by one so able and so honest as Dr Brunton. The thing looked so improbable, that it was considered to be not worth the trouble of discussion. Why it had this appearance of improbability it is easy enough to see. All evidence pointed to the conclusion that infectious diseases were due to the introduction into a higher organism of one or more self-

[1] Probably this was Toussaint.

multiplying lower organisms or their germs. The disturbance to the individual infected (a disturbance manifested to the observer by certain symptoms) might be the result either of the excessive multiplication of the lower organisms, *i.e.*, to their mere numbers, or to the action of chemical substances which they produced, or to both. But, whatever the cause or causes, it seemed certain that the lower organism and the chemical substance must be existing for a long time together in the same blood or tissues, and that this latter therefore, *i.e.*, the chemical substance, could not be an antidote or antagoniser of the former, or, in other words, a disinfectant. Hence, it seemed useless to expect much from it as a preventive, and all efforts were consequently directed towards discovering either some material which, when introduced into the blood, would be incompatible with the growth of the infecting organism, and yet at the same time not incompatible with the continued existence and multiplication of cells and other components, on the activity and integrity of which health and life depended; or else some method of producing with safety a similar protective modification to that produced by the disease itself, by the actual introduction in gradually increasing numbers of the very organisms which caused the disease. Neither alternative was hopeful. The first seemed likely to be useless, the second dangerous, while what might have been an alternative to either of these was condemned beforehand as little other than ridiculous, and we are all of us apt to be so strongly under the tyranny of the prevailing ideas of our time, that we generally prefer to assume an attitude of despair, or to pursue a practice that is attended with risk if either of these harmonises with such ideas, rather than even tentatively to adopt methods and principles which seem opposed to them. Yet there was no reason for despair, for facts were every now and then coming to light—the bye-products, as it were, of inquiries dedicated to other ends, and sometimes disregarded, as residual phenomena too frequently are—which at any rate showed how greatly the virulence of any given bacillus could be mitigated by slight, and what, but for the experiments demonstrating their effectiveness, would have been judged perfectly useless differences in the conditions of development. As an illustration of such mitigation may be related an incident which occurred in the course of Dr Klein's[1] experiments to determine the influence of perchloride of mercury on bacillus anthracis and its spores. He prepared a nutritive medium of Agar Agar, meat extract, peptone, and salt, and inoculated two sets of tubes containing this mixture with the blood of a guinea-pig, dead of virulent anthrax. The mixtures in the two sets of tubes were made with similar proportions of portions of the very same materials, only that for one set was made at a different time from that of the other, and for sterilisation purposes one happened to be boiled longer than the other. "When they came to be used, one set was darker than the other." Anthrax bacilli grown on these two, and then inoculated into guinea-pigs, differed greatly in virulence. That grown on the light-coloured mixture killed by the end of the second or beginning of the third day; that on the dark mixture not earlier than the end of the sixth, or even of the seventh, day.

Happily, however, neither the apparent uselessness, nor the danger, nor the absurdity of either principle, has prevented a tentative application of each to practice, only the one involving the risk of absurdity, while it involved no other risk, has been delayed to the very last. What this is, and the hope that it engenders, I will mention in a moment. I desire firstly, however, to remind you that its application was retarded by what seems to have been a real discovery, which, whether it has the importance attributed to it or not, so exactly fell in with the current ideas of infection, and seemed so effectually to shut the door against the entry of other, and especially of opposing, ideas, that the wonder is that anybody has had the temerity to suggest a new departure. I allude to the demonstration by Metschnikoff of the multiplication within the transparent tissues of such animals as Daphne, of microscopic organisms which had found their way thither. He watched the spores of *Monospora bicuspidata*—a kind of yeast—pass from the in-

[1] *Sixteenth Report of Local Government Board for* 1886–87, pp. 443–4.

testinal canal into the body-cavity. Of course, that as a fact, and a very interesting and novel, or at least newly-observed, fact, was entitled to every consideration. He also saw that, very frequently indeed, in no less than 80 per cent. of the cases observed, the Daphne was very little, if any, the worse for this. But he saw more than this. He observed that the spores, the moment after they had passed into the tissues, were joined by leucocytes, the leucocytes occasionally first of all coalescing so as to form a plasmodium, and the result of the junction of the leucocytes and spores being sometimes the disappearance of the spores, and sometimes the disappearance of the leucocytes and the increase of spores. That[1] is really all that he saw, but that is not the language in which he describes it. What he says he saw is that the spores which passed into the body-cavity were *attacked* by one or more leucocytes, that when those were numerous enough and strong enough, as they were in 20 per cent. of the animals observed, they *destroyed* and *digested* the spores, but that when, on the other hand, the spores were numerous enough and strong enough they *destroyed* and *digested them*, the result in that case being that the spores went on multiplying, until, having destroyed all the leucocytes, they ended by destroying the Daphne. Extending his researches to other animals, and observing analogous phenomena in them, he constructed an elaborate theory of infection. The cells resisting the invading spores are "phagocytes," some of them large ("macrophages"), and others small ("microphages"), and infection occurs, to use the author's own words, "in consequence of a kind of refusal of the phagocytes of a given species of microbes," or, as he further expresses it, rapidly changing the figure, and at the same time trying to overcome what seems to be a very formidable objection, "of a dyspepsia of these cellules (*i.e.*, the phagocytes) in maladies such as tuberculosis or the septicæmia of mice, where the bacilli are englobed, but not destroyed by the phagocytes,"[2] *i.e.*, the leucocytes may decline the combat with the microbes,

[1] *Annales de l'Institut Pasteur*, vol. i. p. 323 *et seq.*
[2] *Ibid.*, p. 334.

in which case there is infection; or, devouring them, they may find that the englobed microbes first cause them dyspepsia, and then end by destroying them, in which case also there is infection: the only escape from this result being when the leucocytes actually fight, kill, and digest the invaders. I am not disputing any facts that were actually observed and that are roughly depicted on these diagrams. I am not even suggesting that ultimately the inference necessarily involved in the employment of such terms as "attacking," "destroying," and "digesting" may not turn out to be correct.

I merely say that these terms were not absolutely required in order to describe what was seen, and that they involve ideas which might be true or might be false. However, they so closely fitted in with the current notions concerning the universal struggle for existence, and the order of development of cases of infectious diseases, that they were eagerly accepted at once as an illustration of that struggle and an explanation of that order. Thus, a person subjected to a distinct infection like that of small-pox, as, for example, by visiting a sick relation in a distant part of the country, his own residence and district being free from the disease, does not at once sicken. Unlike an intoxication as by a poison, such as arsenic or opium, when the effects are speedy and always proportional to the dose, a certain time here elapses before the effects show themselves, and these effects may seem out of all proportion to the supposed dose. The inference, a very probable one, being that in the latter case the incubation stage was one in which the germs were multiplying up to the amount necessary to seriously disturb the functions, when and when only the symptoms characteristic of the disease showed themselves. This reasonable supposition was just what to many minds Metschnikoff's observations converted into absolute demonstration, with the result that prevention was, as I have said, narrowed down to the introduction of a something which would actually kill the lower organism at the risk of killing the phagocyte also; or to a something which should so change the blood and tissues—the culture medium for the time being of the lower organism—as, while not interfering with their own healthful life and activity, would yet make them unfit for supporting the intruding microbes. Allow me to draw your attention for a moment to certain normal processes very similar to those witnessed by Metschnikoff, which have been, and are being observed hundreds and thousands of times in a great variety of organisms, vegetable and animal, but which would sound very strange if deseribed in his language. Spermatozoa, or some of their thousand representative forms, meet with ova or some of their thousand representative forms; they swarm round them, by and by they disappear, and a something results which, under favourable conditions, enters on a long series of developmental changes, often with strange intervening stages, before the cycle is completed. We should be somewhat startled if the embryologist informed us that the spermatozoa, instead of aeting jointly with the ovum to produce a eommon end, were attacked by it, and, though the struggle for existence was sharp, were ultimately overeome, destroyed, and digested. Yet, if in describing what one sees one is entitled to use language whieh, as well as doing that, describes also what one imagines to be the cause of what is seen, there would be no more impropriety in such a description than there may possibly be in Metsehnikoff's.

The evidenee in support of the new order of ideas to whieh I have referred comes from various quarters. It is supplied by competent men working nearly simultaneously with different chemical agents and different methods on different animals suffering from different infective diseases, and yet it all tends to establish the same conclusion, viz., the possibility of affording protection against various kinds of infeetion by the employment of merely ehemical agents. Eaeh witness, therefore, unconsciously strengthens the testimony of all the others, and thus renders it probable that the principle is a sound one, for if one were mistaken it is not likely that all would be.

The first work that I will briefly mention is that of Dr Cash, and I will relate one or two of his experiments, which fairly illustrate my meaning, in his own words:—

"A large rabbit, weighing 3010 grammes, reeeived hypodermically in the course of seventeen days a total of ·0125 gramme of corrosive sublimate" (about $\frac{1}{8}$ grain in the seventeen days, or $\frac{1}{136}$ grain per day). "It was then inoculated with fresh anthrax blood of a guinea-pig, which had succumbed to the disease in 40 hours. . . . . A second unprotected animal was inoculated at the same time, and died of typical anthrax on the evening of the third day."

The protected animal had only a moderate rise of temperature. It lived, and was re-inoculated more than four months after the first inoculation without injury, a control animal submitted to a similar inoculation rapidly dying.

Another protected rabbit was inoculated with the fresh blood of a guinea-pig dead of anthrax, and on the 3rd, 4th, and 5th days after the inoculation its own blood was carefully examined, and on the two latter days unprotected guinea-pigs were inoculated with it. Both experiments were negative. No bacilli were found from the examination, and the guinea-pigs were unaffected.[1] Would not these experiments, even if they stood alone, be sufficient to stimulate inquiry and excite hope? They do not stand alone, yet the necessity of continued inquiry is shown by the next chapter in this history. It is that contributed by Dr Klein.[2] Adopting a different method, he found that bacilli of anthrax could have their virulence so diminished by being grown in medicated culture media containing proportions of corrosive sublimate varying in amount according to the proved virulence of the bacilli, their spore-containing or sporeless character, &c., as to be capable of injection into different animals without ill effects. But he found that what would destroy the virulence of bacilli of one disease would not impair that of those of another, so that the chemical antagonisers of each must be sought by actual experiment.

Facts of this kind cannot fail to engender hopes that we may one day be able to antagonise the cause of a fever by chemical means, *i.e.*, actually to cure the disease. Up to the present time any anticipation of the kind has been thought chimerical.

[1] *Thirteenth Annual Report of the Local Government Board.*
[2] *Ibid.*, p. 156 *et seq.*

Distrust of the possibility of this was justified by all the known facts a few years ago, but the frequent discovery of new and powerful disinfectants, and of the possibility of introducing some of these into the blood in massive doses without injury, must make us increasingly cautious how we adopt the older language and ideas of despair, as though they were justified in the new and more hopeful circumstances of our own day.

But the direction in which this chemical antagonism may be hopefully sought has been indicated by late observers. It is the direction which Dr Brunton considered it but little useful to take.

A remarkable and most encouraging communication was made to the Paris Academy of Sciences, on 20th August of this present year, by a Russian physician, M. Gamaleia, who at several times had worked in Pasteur's laboratory from the year 1886, when he had been commissioned by the municipality of Odessa, at the request of the Society of Physicians of that city, to study there the practice of preventive inoculation against rabies. Briefly, this communication is as follows:—Ordinary cultures of choleraic microbes are so little virulent, that Koch came to the conclusion that cholera was not inoculable into animals. But by passing these first of all through a guinea-pig they become most intensely virulent, and kill pigeons, producing in them a dry cholera, with exfoliation of the intestinal epithelium. The microbe appears in the blood of the pigeons, which, after a few passages, becomes so powerful that a dose of one or two drops kills every pigeon into which it is injected in from eight to twelve hours. It has the same effect on guinea-pigs. But now comes a startling result. Koch failed to give cholera by inoculations with the common bacillus. Yet by inoculating a pigeon twice with an ordinary non-virulent culture of cholera, it was rendered absolutely secure from infection by the virulent blood which had killed every unprotected bird. And this was not all; for, by first of all cultivating the virus in a nutritive medium, and then heating it to 120° C. for twenty minutes, so as absolutely to destroy every contained microbe, a very active chemical substance is left in the sterilised culture, which in large doses will kill in from twenty to twenty-four hours, but in small successive doses will be entirely inoffensive and innocuous, and yet give absolute immunity against the induction of cholera by even large doses of the virulent blood. Can this be true? If so, the principle is established that, by a purely chemical vaccination admitting of rigorous dosage, the effect of which can be predicted with as much certainty as a dosage by arsenic; and by introducing quantities "small enough to be entirely inoffensive, while the sum of these gives the requisite amount," an absolute immunity can be afforded against another of the most deadly diseases known. That the author believes in it is proved by his offer to repeat all his experiments before a commission of the Academy; to submit his own body to inoculation after previous protection; and to proceed to any country ravaged by cholera to establish its efficacy. It seems almost too good to be true. And yet it does not stand alone as we have seen. But Dr Cash's is not the only corroborative testimony to the soundness of this great principle. In the December number of the *Annales de l'Institut Pasteur* for 1887, a similar immunity is claimed to have been obtained by purely chemical vaccination against septicæmia by MM. Roux and Chamberland;[1] while almost at the same time Dr Salmon, in the "Annual Report of the Department of Agriculture of the United States of America," claims to have given pigeons immunity against hog cholera by injections of sterilised cultures of the microbes of that malady. But, to use the words of M. Pasteur, uttered in August of this year, "discoveries accumulate in that which relates to chemical vaccinations. It cannot be doubted that we shall soon possess many others." The following experiment makes it hopeful that already one may have been discovered for hydrophobia. Two dogs, treated firstly by M. Eugène Viala in Pasteur's laboratory, with what appears to have been a purely chemical substance derived from the cord of a rabbit of the 171st passage, dead of rabies, were trephined and inoculated on the 23rd of May of this year with the bulb of a dog, dead of furious rabies, the two dogs continuing quite well on 20th August. Lastly, for yet another malady, and by yet

[1] *Annales de l'Institut Pasteur*, vol. i. p. 561 *et seq.*

another method, has the same principle been established. The experimenter this time was Bouchard,[1] and the details are given in the *Comptes Rendus de l'Académie des Sciences* for 4th June of the present year. The method was as follows:—A series of animals were inoculated with the bacillus of blue pus, and the urine passed by them until the time of their death collected and filtered through porcelain. To make quite sure that no microbes were present in the urine, it was sown in culture media, but with absolutely negative results. Some of the urine thus free from organisms was then injected every second day into three rabbits, which received 205 c.c., 145 c.c., and 140 c.c. respectively. One rabbit was killed by an accident, the other two, at the end of from twelve to fifteen days, were affected with a paralysis of the posterior limbs, exactly like what is produced by inoculating under the skin the pyocyanic microbe. Later on these two rabbits, together with two control rabbits, were submitted to an intravenous inoculation of about 1 c.c. of a culture of the pyocyanic bacillus. The control animals died speedily, the other two remained well. This experiment not only proves that the chemical product of the pyocyanic bacterial life is protective against the disease; it proves that it is *it* and not the bacterium which causes the symptoms; and lastly, it proves that some if not all of the toxic product is eliminated by the kidneys, and thus affords another instance of the advantage and necessity of a much more extended and critical examination of the urine in disease than we have been accustomed to make.

Can all these men—some of the ablest in their several walks—be deceived? If not, we may look forward confidently to the discovery before long of a purely chemical product obtained from cultures of the tubercle bacillus which shall protect those into whom it is inoculated from tuberculosis without itself inducing the disease.

And really, when we reflect on some of the facts of microbic life and of fermentation in general, these results ought not to surprise us, or the attempts to produce them be regarded as unpromising.

[1] *Comptes Rendus de l'Academie des Sciences*, vol. cvii. p. 435.

They should rather fall in with our expectations. For what do we constantly see? Why, that the chemical product of the cell's activity is a poison to the cell itself, or, in other words, that it is an antiseptic to the organism in which the cell lives. In fresh grape juice the yeast plant grows till it has converted the sugar into alcohol, when it can grow no longer, for alcohol is a poison to yeast. But as a matter of fact alcohol is a poison to many cells. Is it therefore unlikely that the chemical product of some specific infective microbe should be poisonous to itself and even poisonous to others, and that by introducing it into a new soil it should prevent the growth of specific infective bacteria if they should be also introduced into the same soil?

But here it is impossible to help indulging in a regret. While all this benevolent activity, so hopeful for humanity, is going on around us, we can take no share in it, but are condemned to be simply chroniclers of its progress. No one can have a greater repugnance to giving needless pain than myself; indeed, I shrink from doing so with feelings akin to horror. Yet it seems to me a disgrace that, in a populous and wealthy city like ours, there is absolutely no opportunity for putting the best considered and most hopeful suggestions for the mitigation of human suffering to the test of an experiment upon any of the lower animals; that, though human beings around us have been bitten by rabid animals during the present year, we have no facilities for producing (and would not dare to avail ourselves of them if we had), by inoculation, a painless disease in rabbits which would give to us always the means whereby we might hope to ward off the fatal event, and secure the victim who is not rich enough to procure a journey to Paris immunity from the fearful sufferings which that disease always entails. I have ascertained that the cost of sending, from this county alone, patients to Paris, and maintaining them there, for the purposes of treatment quite recently would have gone far towards keeping in full working the necessary means of treating all those in it who have been affected. There ought certainly to be established, either in connection with one of our existing hospitals or independently, an institution by which the benefit of Pasteur's method could be offered to those bitten by rabid animals. Five hundred pounds a year would probably be ample for the purpose.

But the rôle of the utility of antiseptic medication is by no means limited to preventive inoculation. As time goes on we shall have to consider the action of many medicines in relation to this principle of disinfection, and to select one or another in particular cases, according as it answers to the principle. Thus we know well the marvellous antiseptic power possessed by some of the compounds of mercury. To the possession of this power is possibly due the special value of calomel as a purgative. Whether that be the case or not, it is certain that it has a special value. It has also a power not possessed by many other purgatives of preventing the decomposition of bile. In proof of this capability of preventing decomposition it is but necessary to examine and compare the specimens of bile on the table. One, to which 3 grains of calomel were added on the 15th September, remains perfectly sweet, while the others, including one which has had nothing added to it, and those with which have been mixed some other of our ordinary purgatives, though put up a fortnight later, have long ago become extremely offensive. While, to illustrate the special value of calomel, I must mention a case or two, merely premising that they are not isolated, but fairly illustrative of a large class.

J. D., blacksmith, was admitted June 8, 1888, suffering from his third attack of rheumatic fever. The two previous attacks lasted for six weeks and four months respectively. He had a florid complexion and reddish hair. Most of the large joints were inflamed. The temperature oscillated between 101° and 103° F. There was free perspiration. A marked feature was constant delirium, intensified at night. Like many florid-faced people, with actively pulsating carotids, he was a busy dreamer even when well. When I saw him I found that a full cathartic had been ordered, together with 15 grains of salicylate of sodium every second hour for four doses, afterwards to be given every four hours, and that the inflamed joints were wrapped in cotton-wool. This treatment was let alone. The symptoms in every respect remaining unchanged on the 10th, 15-grain doses of antipyrin three times a day, with a chloral draught at bedtime, were substituted; but as the delirium continued just as active, the house surgeon applied a large sinapism at the back of the neck. Things were in this state on the 12th, four days after admission. I then prescribed 5 grains of calomel at bedtime. It acted on the bowels but once. The delirium disappeared immediately. The temperature fell very shortly to normal, and though I kept him in for a few weeks in case of relapse, there was no recurrence of symptoms. He left on July 13. He was in bed twelve days.

The next case illustrates a non-febrile class, where calomel was specially useful. Though previously published, it may be mentioned here. Its subject was a robust, healthy-looking man, aged 30, who came into hospital March 30, 1886, complaining of intense pain in the head, most severe in the right temple, but spreading thence all over the head and face, and deafness of the left ear. The headache had lasted, with gradually increasing intensity, for seven months. There was no history of syphilis or ague; but as he had been working in the Mersey Tunnel, and therefore had been much exposed to damp, quinine was administered freely after a preliminary purgative, and a draught containing 16 grains of butyl chloral was given for several nights in succession. A small blister over the most painful spot, 10-grain doses of iodide of potassium, in addition to the quinine, and large doses of chloral hydrate and potassium bromide at night, in place of the butyl chloral, were employed up to the 13th of April without the least benefit, the bowels being regularly cleared by the hospital pills or draught. His suffering was very acute. On the 13th 5 grains of calomel were given. The effect was most gratifying. The headache, which had persisted up to the time of his taking the calomel, entirely disappeared. The dose was repeated on the 17th and 19th, not because there was pain, but to relieve the bowels. He slept well every night, and, having been free from pain for a week, insisted on leaving to go back to work on the 21st. In these cases ordinary purgatives had been administered without any benefit. Calomel had actually purged less than they, and yet it produced effects which they could not produce. I am persuaded that the value of this drug is too little appreciated. We all know the extraordinary effect of extremely minute frequently repeated doses—from half a minim to a minim of the official solution—of bichloride of mercury in checking the summer diarrhœa of children; and as this effect runs on all fours with its equally extraordinary antifermentative and antiseptic power, it is not unlikely that the two are connected, and that its use illustrates a general principle of intestinal antisepsis. I some time ago saw this principle designedly and most happily applied by means of another agent in a case of very chronic diarrhœa in an elderly lady under the care of Dr Logan. The evacuations were very frequent, liquid, offensive, from a sickly putrescent odour, and (as was to be expected) swarming with bacteria. Various medicines were administered to no purpose, when it occurred to Dr Logan to give 10-grain doses of boric acid, with the view of sweetening the stools, and possibly by its antifermentative action checking them. It fulfilled both purposes at once. And it will be an interesting point to determine what are the special characters of a diarrhœa which make it controllable by one antiseptic rather than another, or resistant to them all. In some more recent cases, one especially, where in age, chronicity, and frequency and character of the evacuations, the patient closely resembled the one just alluded to, and where I hoped for similarly good results, the acid was given without effect, so that there must be something very special which it influences, but what that something is I do not yet know.

We all know, however, the practical application given to intestinal antisepsis by the experiments of Bouchard, whose mixture of charcoal, iodoform, and naphthalin is so often used where it is designed to prevent the formation of soluble putrefactive products.

Not content with this, he has extended the principle to *internal* antisepsis, at any rate in typhoid fever, choosing as the special agent for this calomel, of which 40 centigrammes (about 6 grains) are given daily in 20 doses of 2 centigrammes (about $\frac{3}{10}$ grain) each, one every hour for four consecutive days.

He makes the following remarks:—"Almost all the medicaments which diminish fever in abdominal typhus are antiseptics. All those which have been reputed specifics or simply considered to be useful are antiseptics: chlorine, iodine, sulphurous acid, sulphites, hyposulphites, mercurials, essence of turpentine, creasote, thymic acid, benzoic acid, salicylic acid, boric acid, iodoform, quinine, resorcine, kairine, antipyrine, thalline. I think, then, that experience has already pronounced, and that practically as well as theoretically, that a favourable effect can be obtained in the course of infectious maladies by the employment of the preceding substances."[1] We must not forget however, that chlorine was recommended strongly many years ago by Schönlein of Berlin, because of its antiseptic power, and that, writing of it in 1873, the late Dr Murchison remarked,—"Of all the remedies belonging to this class, free chlorine has appeared to me to be most useful. . . . . . I have repeatedly found it to have a beneficial influence upon the abdominal symptoms."[2] In stating Bouchard's practice in typhoid fever, my object was merely to show how largely the principle of disinfection is occupying the minds of some, and not from any experience in his special method of employing calomel in order to carry it out. His own judgment on this method is, that it shortens the mean duration of the disease from twenty-five to twenty-one days, that it reduces the mortality (two deaths in thirty-two cases), but that the convalescence is prolonged and attended by debility and great anæmia—very serious drawbacks certainly.

The careful antisepsis of every mucous membrane, such as that of mouth, throat, &c., capable of lodging specific poisons, is now commonly practised, and a new impetus and direction should be imparted to this practice by the relationship apparently established quite recently between some simple ulcers of the stomach or duodenum and infective ulcers or abrasions of the lower bowel or uterus. It seems a long way to go to a part so remote as the uterus or the vagina for an explanation of the cause of chronic ulcer of the stomach; yet, puzzled as we often

[1] *Leçons sur les Autointoxications dans les Maladies*, p. 215.
[2] Murchison on *Fevers*, 2nd ed., p. 645.

are to account for the origin of this affection, it may not be unwise to bear in mind such cases as the following, which occurred to M. Letulle:—In a patient suffering from puerperal septicæmia two recent hæmorrhagic ulcerations of the stomach occurred. The patient died. The venous sinuses of the uterus were crammed with colonies of Streptococci. On examining the venules subjacent to the stomach ulcers, they were found thrombosed, the fibrinous clots containing a great number of the same Streptococci. Another patient, a male, aged 28, contracted dysentery in Cochin China. Three times in the course of thirty-two months, after his return home, he suffered relapses. A month after the last attack he had hæmatemesis, severe epigastric pain, and the other symptoms of gastric ulcer. The blood-stained dejections of a still later attack of dysentery being cultivated in M. Cornil's laboratory, gave the microbe that has been described by Chantemesse and Widal as pathogenic of dysentery, and "pure cultures of these germs inoculated into the guinea-pig reproduced the specific lesions of the intestine, and *twice occasioned ulceration of the stomach.*"[1] What is the moral of all this? Here was a case where, the character of the infecting organism being consistent with years of life, there occurred renewed outbreaks of the disease after apparent cures, and later on an ulceration at a part remote from the one first attacked. In the other case an organism of a character highly dangerous to life, planted in the uterus or vagina, made its way somehow to the tissues subjacent to the mucous membrane of the stomach and caused ulcer of that organ. In some other case it may be an organism, as little likely to be rapidly fatal as that which causes dysentery, that might light upon the vaginal or uterine membrane, and hence be conveyed (as the microbe in the first case was from the bowel) directly or indirectly to the stomach. Are we not often wholly at a loss to get at the cause of chronic ulcer of that organ? But we do know that it frequently is associated with ulcerations of the skin, such as those of syphilis or tubercular affections and with uterine disorders, and especially that it occurs with great frequency in females,

[1] *Comptes Rendus de l'Academie des Sciences*, vol. cvi. p. 1752.

though rarely, even in these, before menstruation has been established. The moral, then, seems to be—(1) An extension of the practice so ably recommended and supported by so many startling facts in last Saturday's *British Medical Journal*, by Dr Cullingworth, with reference to the prevention of puerperal fever. I would venture to say that, in all cases whatever requiring vaginal or intestinal examination, and not merely in puerperal cases, the finger or instrument should be disinfected in the way recommended by him. Indeed, I would carry the principle still further, and say that every wound or scratch of the surface, however trivial, should be antisepticised. (2) That in case of unhealthy uterine or vaginal discharges occurring concurrently with chronic gastric ulcer, the systematic employment of antiseptic douches might reasonably be recommended at the same time that non-irritant antiseptics might be given by the stomach. (3) That antiseptics might advantageously be administered in dysentery, especially if gastric pain should indicate the extension to the stomach of the process described by Letulle. The healthy stomach is itself an antisepticiser, and it is not likely that any of the numerous bacteria that must constantly be conveyed into it with the food would stand much chance of a long enough survival to do mischief. Their only chance seems to attack it from its outer side, and, as Letulle's cases show (strange as it may seem), they can sometimes do this successfully. I remember distinctly the marked amelioration brought about in a very bad case of dysentery, under treatment in hospital a few years ago, by the administration of large doses of liquor chlori. It was objected to me that it could not do any good, as it would enter into combination long before it could reach the desired part. That seemed to be a sound objection, but in spite of it I gave the medicine, and the medicine gave the benefit. My surprise at this has been considerably lessened on my reading a short time ago, in the most recently issued volume of the "Local Goverment Board's Reports," that Dr Cash had determined that "1 part of chlorine water containing $\frac{3.5}{1000000}$ grm. of Cl is sufficient to destroy, within five minutes, one-fiftieth part of its bulk of anthrax blood," so that guinea-pigs could be inoculated with the mixture without the slightest evil result.

Closely related to the antiseptic management of the puerperal woman, so strongly insisted on by Dr Cullingworth, should be that of the infant; for, whatever opinion we may as yet entertain concerning the contagious nature of tetanus, there cannot now be much doubt as to that of trismus nascentium. Many probably have read the following case, reported at p. 159 of the first volume of Sajous's *Annual of the Medical Sciences*:—An infant became tetanic five days after birth and a day and a half after the falling off of the cord. "The navel wound did not exhibit anything unusual; it was covered with a slight suppuration." The symptoms rapidly developed and the child died, when, the navel being excised and mice inoculated, these rapidly became tetanised. Guinea-pigs being then inoculated from the mice, they in their turn became tetanised and died. Nothing is said of the actual demonstration of a microbe. The sound practical conclusion come to, however, by the reporter, is that "prophylaxis imperatively demands a careful antiseptic treatment of the navel wound" in all cases.

But we shall have to go yet further in our study of the altered chemistry of disease, and the way to modify it. Several significant facts, of which the following are examples, seem to be firmly established by modern physiology—viz., (1) That a considerable portion of our tissues (not less, it is thought, than one-fifth) live their life, like certain microbes, anaërobically. We were so accustomed to consider all nutritive and disassimilative changes going on within the body as changes of oxidation, that it seemed difficult to believe that not a few, at any rate of those of disassimilation, whereby the tissues were reduced to simpler gaseous or liquid combinations capable of being eliminated, were strictly analogous to putrid fermentation, and not only did not require free oxygen for their production, but would be actually checked or prevented by it. A second important fact is, that the products of tissue change which result from free oxidation are harmless as compared with those which take place without oxygen. When the body is working healthfully, there is never such an excess of the putrefactive or anaërobic products within it at any one time as to prove a source of danger. In acute specific fevers, however, and probably in febrile disorders of inflammatory origin, both processes are stimulated, and both go on in excess of what is normal. Our attention, however, has up to the present time been almost exclusively directed to the former or least harmful process, and we have thought little or nothing of the latter. Yet, except as an index of the degree to which oxidation is going on, the determination of the amount of urea, water, and carbonic anhydride, the end-products of that oxidation, is of minor importance in this relation, as none of these compounds can properly be called poisonous. That which causes re-breathed air to be so injurious is not the CO_2 it contains so much as the minute proportion of a highly poisonous organic chemical substance, giving many of the characters of an alkaloid, examined and described by MM. Brown-Séquard and D'Arsonval in the *Comptes Rendus de l'Acad. des Sci.*, Jan. 9 and 16, 1888. What we want to know is the extent to which anaërobic cell-life is stimulated in fever, to what degree the poisonous products that usually in small proportion accompany its activity are thus increased, and if any means can be discovered by which the activity of the injurious cell-life can be repressed while oxidative cell-life is allowed to go on.

That is one of the problems of the future, and, though a very difficult one, it cannot certainly be considered incapable of solution.

To prevent the possibility of any misconception, I wish to remark here, as it were in parenthesis, that I must not be considered to take the low view of regarding man as nothing more than a material laboratory for the genesis of various forces. I believe that he is a spiritual being, whose hopes, and fears, and griefs, and aspirations cannot be resolved into the mere play of mechanical and chemical forces; but I believe also that it is our duty, and should be esteemed our privilege, to extend our investigations to the utmost attainable limits into the processes going on in his tissues and organs, and into the mechanism by which they are effected.

And, from what has already been done, we cannot fail, I think, to be struck with the similarity between the chemical changes taking place in living cells everywhere—whether these cells be isolated organisms or parts of a higher and more complex structure.

As has been said, with probably a considerable measure of truth, by a recent writer, "Bacteria and cellules, superior in organism, are able to live the same kind of life, following the same laws, leaving as residues of their activity the same principles equally toxic for all."[1] Herein is the justification for that careful observation of the conditions that modify the life and growth of the anaërobic bacteria which is now being made by bacteriologists. The fruit will be gathered by and by when we who practise medicine have placed in our hands (as we surely shall have) the means by which the undue and injurious activity of the anaërobic cells of our own organism can be repressed.

Results succeed each other very quickly, and it is but a few weeks since the novel fact in physiology was announced and established of the power possessed by certain plants of consuming intracellular sulphur without the intermediation of oxygen, and of forming directly at its (the sulphur's) expense not only H_2S but also a sulphur substitute of an isomer of urea, in which sulphur takes the place of oxygen; "this fact, absolutely new, seems," to use the words of M. Olivier, who announces it, "to assign to sulphur a function of which we knew up to the present time no example in physiology." But what gives more especial interest to us is the further fact, still more recently discovered, that a substance,[2] possessing the power of bringing about a direct union between sulphur and hydrogen at ordinary temperatures, is very widely diffused throughout the living tissues and cells of animals. Something has already been done to determine the conditions under which its activity can be stimulated or repressed; and when we remember that the end-product of the oxidation of hydrogen, viz., water, is absolutely harmless, but that the corresponding product of the combination

[1] L. Hougounenq, *Les Alcaloïdes d'origine animale*, p. 88.

[2] M. J. de Rey Pilhaide terms this substance "philothion."

between sulphur and hydrogen is extremely poisonous, and when we further bear in mind that we always have within us a substance capable, under favourable conditions, of rapidly determining this combination, we shall see the importance of possessing the means of repressing its activity on the one hand, while we promote that of oxidation on the other. This, when we have it, will be another advance in the application of the principle of disinfection in medicine, for it is only by an antiseptic or disinfectant yet to be discovered that the result will be obtained. When it is attained we shall see fewer of those cases, until recently quite inexplicable, where, in the course of a chronic ailment of no great severity, the patient almost suddenly sinks, overwhelmed by the action of a self-generated and non-eliminated poison.

The statement that I have made as to the position which disinfection should take in medicine, though long and tedious, is not—as indeed it could not be—a complete one. The subject has grown, and is still growing, so rapidly, that all that can be done is to draw attention to it by citing some examples of its importance. Very soon we shall have to make an entire re-arrangement of our medicines in relation to this single principle of disinfection, which will certainly become a prominent part of the therapeutics of the future; and he will be at once the most practical as well as the most scientific medical man who shall fully accept the spirit of the new teaching, and most fully apply its principles in his daily work.